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PATENT
Attorney Docket No. 208250
DHHS Reference E-190-98/2

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Ho et al.

Application No. 09/743,873

Group Art Unit: 1624

Examiner: B. Kifle

Filed: April 18, 2001

For: WATER-SOLUBLE DRUGS AND RELATED COMPOSITIONS AND METHODS OF PREPARING AND USING SAME

AMENDMENT AND RESPONSE TO OFFICE ACTION

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

In response to the Office Action dated September 6, 2002, please enter the following amendments and consider the following remarks.

AMENDMENTS

IN THE SPECIFICATION:

Please replace the paragraph on page 1, lines 13-33, with the following:

A common problem associated with drugs intended for parenteral, and especially intravenous, administration has been the solubilization of a slightly soluble or water-insoluble active ingredient (Sweetana et al., *PDA J. Pharm. Sci. & Tech., 50*, 330 (1995)). As a result, many drugs of potential benefit in cancer chemotherapy and other areas of therapeutics have been abandoned. Methods have been developed whereby drugs can be enveloped in micelles and placed into aqueous solutions (Hawthorne et al., *J. Neurooncol., 33,* 53-58 (1997)). Likewise, cosolvents and complexing agents allow some drugs to be dissolved in water (Badwan et al., U.S. Patent No. 5,646,131). The use of these reagents, however, can be complex and have negative attributes due to the additional reagent required to dissolve the active ingredient (Sweetana et al. (1995), *supra*). Prodrugs also have been developed by attaching groups, such as phosphates and other conjugates, to increase their solubility and enhance their performance (Schacter et

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AMENDMENTS TO SPECIFICATION
MADE IN RESPONSE TO OFFICE ACTION DATED SEPTEMBER 6, 2002

(Deletions are indicated by bracketed text, while insertions are indicated by underlined text)

Please replace the paragraph on page 1, lines 13-33, with the following:

A common problem associated with drugs intended for parenteral, and especially intravenous, administration has been the solubilization of a slightly soluble or water-insoluble active ingredient ([Sweetna] Sweetana et al., *PDA J. Pharm. Sci. & Tech., 50,* 330 (1995)). As a result, many drugs of potential benefit in cancer chemotherapy and other areas of therapeutics have been abandoned. Methods have been developed whereby drugs can be enveloped in micelles and placed into aqueous solutions (Hawthorne et al., *J. Neurooncol., 33,* 53-58 (1997)). Likewise, cosolvents and complexing agents allow some drugs to be dissolved in water (Badwan et al., U.S. Patent No. 5,646,131). The use of these reagents, however, can be complex and have negative attributes due to the additional reagent required to dissolve the active ingredient ([Sweetna] Sweetana et al. (1995), *supra*). Prodrugs also have been developed by attaching groups, such as phosphates and other conjugates, to increase their solubility and enhance their performance (Schacter et al., *Cancer Chemother. Pharmacol., 34,* S58 [(1993)] (1994); Kingston et al., U.S. Patent No. 5,278,324).